47

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,605	09/12/2001	Robert Ian Lechler	5585-59112	2755

24197 7590 04/08/2004

KLARQUIST SPARKMAN, LLP
121 SW SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,605	LECHLER ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,5-9,12-15,24,25,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 2, 5-9, 12-15, 24, 25, 27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 20010619
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of applicants election with traverse of the Group comprising a single B-cell epitope derived from CD86. After review and reconsideration of the prior art with respect to the instant amended claims, the restriction requirement is withdrawn.

Claims 3, 4, 10, 11, 16-23 and 25 are canceled. Claims 2, 5, 9 and 25 have been amended. Claims 1, 2, 5-9, 12-15, 24, 25, 27 and 28 are pending and examined on the merits. Claims 1, 6, 7, 8, 14, 15, 24, 25 will be examined to the extent that they read on a B-cell epitope from porcine CD86.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) Claims 5 and 12 are vague and indefinite for reliance upon a figure. The M.P.E.P (2173.05(s) states

Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

(B)Claims 2 and 9 vague and indefinite in the recitation of "derived from" CD86. It is unclear if "derived from encompasses structural changes imposed porcine CD86 or a CD86 fragment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-9, 12-15, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Etlinger (EP 429,816) in view of Maher et al (Journal of Immunology, 1996, vol. 11, pp. 3838-3844, reference of the IDS filed June 19, 2001)

Etlinger teaches a method for inducing a humoral response comprising the administration of an antigen which comprises a B-cell epitope linked to a carrier protein, wherein said carrier protein comprises a T-cell helper epitope devoid of T suppressor function (page 2, lines 17-25 and page 4, lines 14-28 and page 4, line 49 to page 5, line 9) fulfilling the specific embodiment of claim 15, drawn to a carrier. Etlinger teaches examples of carrier proteins as de-toxified tetanus toxin or diphtheria toxin, thus fulfilling the specific embodiment of claims 6 and 14 drawn to a tetanus toxoid (page 2, lines 27-30). Etlinger teaches that the B-cell epitopes are capable of inducing the formation of antibodies which bind to the native molecule in a host (page 2, lines 18-22). Etlinger teaches that in general B-cell epitopes comprise at least 6 amigo acids and that larger fragments may represent more than one epitope or overlapping epitopes

(page 6, lines 37-42). Etlinger does not teach a vaccine comprising a B cell epitope of porcine CD86 linked to tetanus toxoid, nor a method for improving tolerance to a xenograph

Maher et al teach that porcine endothelial CD86 is a major co-stimulator of xenogenic human T-cells (title) fulfilling the specific embodiment of a porcine polypeptide expressed by vascular endothelial cells of a xenograph. Maher et al teach that in the case of transplanted vascularized solid organs, graft endothelial cells may serve both as targets and as the Ag-presenting cells that initiate host-antigraft responses (page 3838, first column , last sentence). Maher et al teach that porcine endothelial cells interact with human T-cell CD28 providing a co-stimulatory response that could be blocked by anti-CD28 antibodies or CTLA-Ig fusion proteins (page 3838, second column, lines 14-16). It is known in the art that CD86 is synonymous with B7.1, and that B7.1 interacts with the T-cell receptor at CD28 (Paul, fundamental immunology...). It flows logically from this that if antibodies to CD28 can block the interaction between the CD86 or the porcine endothelial cells and the CD28 of human T-cells, then antibodies to porcine CD86 can also block the interaction between CD86 on porcine endothelial cells and CD28 of human T-cells.

It would have been prima facie obvious to one of skill in the art at the time the invention was made to administer an antigen comprising a B-cell epitope of the extracellular domain of porcine CD86 and a T-helper cell epitope of tetanus toxoid to an individual receiving a porcine vascularized organ. One of skill in the art would have been motivated to do so by the teachings of Maher et al regarding the ability of CD86 on porcine endothelial cells to activate human T-cells, and the teachings of Maher et al that blocking of said interaction by the administration of anti-CD28 antibodies and prevent stimulation of the human T-cells. As stated above, it flows logically from this that blocking of the CD86 CD28 interaction with anti-CD86 antibodies would also prevent the stimulation of t-cells. further, one of skill in the art would be motivated to choose a B-cell epitope from the extracellular domain of porcine CD86 because of the teachings of Maher et al which indicate that the graft endothelial cells are serving as antigen -presenting cells. One of skill in the art would realize that only the extracellular domain of CD86 would be accessible for interaction with human T-cells and thus, antibodies which would bind to the intracellular domain would interfere with the activation of human T-cells. It would be further obvious that the administration of at least 9 amino acids of CD86 would guarantee that at least

one B cell epitope was present in the antigen, as Etlinger teaches that an antigenic determinant comprises at least 6 ammo acids.

Claims 1, 2, 5-9, 12-15, 24, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maher et al and Etlinger as applied to claims 1, 2, 5-9, 12-15, 27 and 28 above, and further in view of Muller et al (WO 97/11971, reference of the IDS filed June 19, 2001).

Claims 24 and 25 embody the methods of claims 1 and 7, respectively wherein said B-cell epitope has less than 75% sequence identity to a corresponding region of an equivalent human polypeptide.

Muller et al teach a method for treating rejection of a xenographed organ, tissue or cell comprising administering and antibody which binds to porcine CD86 but not to human CD86.

It would have been prima facie obvious at the time the invention was made to administer a B-cell epitope from porcine CD86 which has less than 75% sequence identity to the corresponding region of an equivalent human CD86. One of skill in the art would have been motivated to do so in order to elicit antibodies which would bind to porcine CD86 but not to human CD86.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Gimmi et al, PNAS, 1993, Vol. 90, pp. 6586-6590;

Lenschow et al, Transplantation, 1995, Vol. 60, pp. 1171-1178;

Ho et al, European Journal of Immunology, 1990, vol. 20, pp. 477-483;

Valmori et al, Journal of Immunology, 1992, Vol. 149, pp. 717-721.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
Art Unit 1642
04/05/04

KAREN A. CANELLA PH.D
PRIMARY EXAMINER